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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/840,795	04/23/2001	Erin E. Murphy	SF0818KQ	5250

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EXAMINER
O HARA, EILEEN B

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 11/27/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/840,795	MURPHY ET AL.	
	Examiner	Art Unit	
	Eileen B. O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-10 and 16-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-20* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Formal Matters

1. The Attorney Docket Number has been changed as requested by Applicants in the paper received Sept. 30, 2002.

Status of Claims

2. Claims 1-20 are pending in the instant application.

Election/Restriction

3. Applicant's affirmation of election with traverse of Group C, drawn to a binding compound comprising an antibody binding site and method for detecting protein, claims 11-15, and Group VIII, drawn to SEQ ID NOS: 18 and 19, in Paper No. 7 is acknowledged. The traversal is on the ground(s) that no serious burden would exist to examine binding compounds which specifically bind to the polypeptide sequences of Groups VI, VII and VIII.

This is found persuasive because Applicants submitted an alignment of these sequences showing significant overlap. Therefore, binding compounds specific to SEQ ID NOS: 15, 17 and 19 shall be examined together.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-10 and 16-20 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b)as being drawn to a non-elected invention.

Claims 11-15 are currently under examination.

Information Disclosure Statement

4. The sequences disclosed in the IDS filed Feb. 22, 2002 (references AV, BB, BH, BK, BM, BP, BQ and BR) have been considered to the extent that was possible absent an explanation of relevance or a sequence alignment.

Priority

5. This application filed under former 37 CFR 1.60 lacks the current status of the nonprovisional parent application 09/351,777. A statement reading "(now abandoned)" should be included after "09/351,777 filed on July 12, 1999" in the first sentence of the specification.

Specification

6. The disclosure is objected to because of the following informalities: the specification is objected to for referring to SEQ ID NOS: 12-19 as Table 4. The sequences in Table 4 are not in tabular form, and should be presented in a figure or should be deleted, since they are duplicates of the sequence listing.

Appropriate correction is required.

Claim Objections

7. Claims 11 and 12 are objected to because of the following informalities: they recite non-elected inventions. Appropriate correction is required.

Claim Rejections - 35 USC § 101 and § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 11-15 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The elected invention is directed to binding compounds comprising an antibody binding site which specifically binds to at least 17 contiguous amino acids from SEQ ID NOS: 15, 17 or 19, and method of detecting antigen in a biological sample. The instant specification discloses that the polypeptides comprising the amino acid sequences presented in SEQ ID NOS: 15, 17 and 19 are putative receptor molecules of the tumor necrosis receptor (TNFR) superfamily, identified as human RANKL (RANK-Like), based on structural homology to that family of proteins, and are splice variants. The RANKL clones were assembled through analysis of ESTs present in various databases and were identified from several different libraries (paragraph bridging pages 31 and 32). However, the claimed binding compounds and methods do not have any specific and substantial utility, or a well established utility, as determined according to the current Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday, January 5, 2001.

Although the claims are directed specifically toward the binding compounds and method of detecting antigen, the asserted utilities of the nucleic acids and encoded RANKL polypeptides will also be discussed, since they are closely inter-related. The instant application describes the uses and methods of the invention, and state that the nucleic acid molecules can be used to express the encoded protein, and can be used in methods such as isolating a DNA clone encoding

RANKL, such as a RANKL gene from various species, Northern blotting and Southern blotting, in chromosome mapping, defining various cell subsets, and diagnostically or therapeutically. Asserted utilities for the proteins include using the proteins to generate antibodies, use of soluble forms of the receptors as antagonists of the ligand, use in assays to discover natural ligands or compounds that bind to the receptors, drug screening assays, defining various cell subsets, to modulate the physiology of cells, and in diagnostic and therapeutic methods. The specification further asserts that the receptors may provide a costimulatory signal to cell activation, or be involved in cell proliferation or differentiation, and will likely modulate cells which possess the receptors, e. g., T cell mediated interactions with other cell types, which would lead to modulation of cell growth, cytokine synthesis or development of particular effector cells. Asserted utilities for the antibodies (binding compounds) include purifying the protein by affinity chromatography, use of antibodies coupled to toxins or radionuclides to kill cells expressing the RANKL protein on its surface, conjugation of drugs to the antibody binding compounds for drug targeting, use of the antibody binding compounds to modulate the physiology of cells (regulation or development of hematopietic cells, use in methods to detect the protein, for example in diagnostic applications to detect abnormal levels of protein that may be involved in a disease process, and therapeutic uses such as to treat cancer, degenerative or autoimmune disorders.

However, these are not considered to be specific or substantial utilities for either the nucleic acid molecules or the proteins. Some of the asserted utilities, such as Northern and Southern blotting, generating antibodies, detecting protein in a biological sample, and chromosomal mapping are considered general methods that any nucleic acid, protein or antibody could be used for, and are not considered to be specific or substantial utilities. The utilities

described above are general and would apply to any polynucleotide or protein. The asserted involvement of the RANKL receptors in cell proliferation or differentiation or involvement with any disease or disorder is conjectural, and is based on RANKL proteins having common structural motifs with the TNF family of receptors, which as a family are involved in various immune responses, diseases and disorders. Though it is likely that the RANKL proteins are receptors in the TNF receptor family, this does not automatically confer a specific and substantial utility to any new member of the family absent any information about it's possible biological significance.

It is asserted that the RANKL polypeptides are receptors in the TNF family. There is no ligand identified that binds to them, no signaling pathway with which they are involved, and no disease or disorder correlated with the polypeptide. Therefore, the antibody binding compounds do not have any specific diagnostic or therapeutic use. The use of an orphan receptor to discover its ligand or properties does not constitute a specific, substantial utility. Since the instant specification does not disclose how to use the RANKL nucleic acids or polypeptides, a skilled artisan would not know how to use antibody binding compounds to the polypeptides other than in general methods of using the antibody binding compounds to determine what tissues or cells express the protein or to purify the protein. It is possible that, after further characterization, this protein might be found to have a patentable utility, in which case antibodies to the protein would have a specific utility, or the protein might be found to be associated with a specific disease.

In Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct,.1966), a process of producing a novel compound that was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be useful because the compound produced thereby was

potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The instant claims are drawn to antibody binding compounds (and method of binding) to a protein which has undetermined function or biological significance. Until some actual and specific activity can be attributed to the proteins identified in the specification as RANKL proteins or the polynucleotides encoding them, the antibody binding compounds and method of using the antibody binding compounds to form binding compound:antigen complexes do not have a specific and substantial utility.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 11-15 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 11-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10.1 Claims 11-15 are indefinite because claim 11 recites "specifically" binds to, and it is not clear what "specifically" binds to means. This rejection would be withdrawn if the word "specifically" was deleted from the claim.

10.2 Claims 12 and 15 are indefinite because claim 12 recites "selectively" immunoreactive, and it is not clear what "selectively" immunoreactive means. This rejection would be withdrawn if the word "selectively" was deleted from the claim.

10.3 Claims 12 and 15 are indefinite because claim 12 recites in section b) 2) that the binding compound is a polyclonal antiserum, and a polyclonal antiserum is not a compound but is composed of many compounds. The rejection would be withdrawn if the claim was amended, for example, to insert the phrase "present in" before the phrase "a polyclonal antiserum".

10.4 Claim 15 is indefinite because it encompasses a detection kit comprising a binding compound and a compartment providing segregation of the binding compound, and it is not clear what it is being segregated from

11. The art considered pertinent to the present application is Yan et al. Two-Amino Acid Molecular Switch in an Epithelial Morphogen That Regulates Binding to Two Distinct

Receptors. Science, Vo. 290, Oct. 20, 2000, pages 523-527. Yan et al. discloses a polypeptide identified as human XEDAR (see Fig. 1A), which is 99.5% identical to amino acids 1-205 of the polypeptide of SEQ ID NO: 19 of the present application and binds to the ligand EDA-A2. This is not considered prior art, as the paper was published after the effective priority date of the instant application (July 7, 1999).

Conclusion

12. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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Patent Examiner